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Original investigation

Increased prevalence of left ventricular hypertrophy in hypertensive women with type 2 diabetes mellitus

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Abstract

Background: Left ventricular hypertrophy (LVH) is a powerful independent risk factor for cardiovascular morbidity and mortality among hypertensive patients. Data regarding relationships between diabetes and LVH are controversial and inconclusive, whereas possible gender differences were not specifically investigated. The goal of this work was to investigate whether gender differences in left heart structure and mass are present in hypertensive patients with type 2 diabetes.

Methods: Five hundred fifty hypertensive patients with at least one additional cardiovascular risk factor (314 men and 246 women, age 52 to 81, mean 66 ± 6 years), were enrolled in the present analysis. In 200 (36%) of them – 108 men and 92 women – type 2 diabetes mellitus was found upon enrollment. End-diastolic measurements of interventricular septal thickness (IVS), LV internal diameter, and posterior wall thickness were performed employing two-dimensionally guided M-mode echocardiograms. LVH was diagnosed when LV mass index (LVMI) was $>134 \text{ g/m}^2$ in men and $>110 \text{ g/m}^2$ in women.

Results: Mean LVMI was significantly higher among diabetic vs. nondiabetic women (112.5 ± 29 vs. 105.6 ± 24 , $p = 0.03$). In addition, diabetic women presented a significantly higher prevalence of increased IVS thickness, LVMI and left atrial diameter on intra-gender comparisons. The age adjusted relative risk for increased LVMI in diabetics vs. nondiabetics was 1.47 (95% CI: 1.0–2.2) in females and only 0.8 (0.5–1.3) in males.

Conclusion: Type 2 diabetes mellitus was associated with a significantly higher prevalence of LVH and left atrial enlargement in hypertensive women.

Introduction

Patients with overt diabetes and hypertension are exposed

to an exceptionally high risk of cardiovascular death, and are generally thought to need a more intensive risk factor

control [1]. Epidemiologic studies have shown that left ventricular hypertrophy (LVH) is the most powerful independent risk factor for cardiovascular morbidity and mortality in these patients. The prevalence of LVH in patients with essential hypertension is in average 40% (range 12% to 70%), depending to a large extent on the measurement technique used [2-6]. The relationships between glucose metabolism abnormalities and LVH have been described in several reports [7-10]. However, the findings were controversial and inconclusive [11]. The gender differences were not specifically investigated in this issue. The goal of this work was to elucidate whether gender differences in left heart structure and mass are present in hypertensive patients with type 2 diabetes.

Patients and methods

The International Nifedipine GITS Study of Intervention as a Goal in Hypertension Treatment (INSIGHT) Trial has studied hypertensive patients with at least one additional cardiovascular risk factor and thus with a clear-cut elevation in overall risk. The design of the INSIGHT study has been described elsewhere [12,13]. The INSIGHT trial has also conducted a number of side arms in different countries to address several important issues for which information is still limited.

Over the course of 18 months 585 high risk patients with hypertension plus at least one additional risk factor who were recruited to the INSIGHT study in our region underwent echo-Doppler examination. A total of 25 patients dropped out during the recruitment because of the technical reasons (suboptimal echocardiographic images. Therefore, 560 patients (314 men and 246 women, age 52 to 81, mean 66 ± 6 years), were enrolled in the present analysis. In 200 (36%) of them – 108 men and 92 women – type 2 diabetes mellitus found upon enrollment (prevalent diabetes group). The remaining 360 patients without clinically manifested diabetes constituted the nondiabetic group.

The diagnosis of diabetes was made on the basis of the reported history and medical records.

Coronary artery disease (CAD) was diagnosed in accordance with the INSIGHT clinical trial protocol: documented previous myocardial infarction, obstruction equal or more than 70% in at least one of the major epicardial arteries on coronary angiography, percutaneous transcoronary angioplasty or coronary artery bypass grafting, and based on accepted reliable medical records (hospitalization summary and/or coronary angiography protocol).

Echo-Doppler-two dimensional echocardiography

Examinations were performed at baseline with a Hewlett-Packard ultrasound imaging system model SONOS 1000,

1500 or 2500 with a 2.5 and 3.5 Mhz transducer. Standard images were obtained from the left parasternal (long and short axis view), apical (long, two chamber and four chamber) and subcostal views.

Two-dimensionally guided M-mode echocardiograms of the left ventricle (LV) were taken at cordal level, with the patient in partial left decubitus position, and three to five measurements were averaged. End-diastolic measurements of interventricular septal thickness (IVS), LV internal diameter, and posterior wall thickness (PWT) were carried out in accordance with the American Society of Echocardiography recommendations.[14] The left ventricular mass (LVM) was calculated by the formula introduced by Devereux and Reicheck [15] and was indexed for body surface area to obtain the LVM index (LVMI). Left ventricular hypertrophy was diagnosed when LVMI was $>134 \text{ g/m}^2$ in men and $>110 \text{ g/m}^2$ in women [16]. Only frames with optimal visualization of interfaces and showing the septum, LV internal diameter and posterior wall simultaneously were used for reading

All studies were recorded on a super-VHS tape and evaluated by 2 cardiologists with expertise in echocardiography, who were blinded to the presence or absence of diabetes. In case of disagreement, a third examiner was consulted

Statistical analysis

Data were analyzed using SAS software [17]. Comparisons of proportions were made using the chi-square test. Statistical analysis for inter- and intra-gender comparisons was performed using the Student's t test. A p value of less than 0.05 was considered statistically significant.

Results

In inter-gender comparisons, men were older; the prevalence of smoking and proven CAD was significantly higher among them. Duration of hypertension was longer among women (Table 1). No inter-gender differences were found regarding systolic and diastolic blood pressures on inclusion. In patients of both genders (intra-gender comparisons) no differences were found regarding age, systolic and diastolic blood pressures on inclusion, duration of hypertension and prevalence of CAD. However, mean LVMI was significantly higher among diabetic women (112.5 ± 29 vs 105.6 ± 24 , $p = 0.03$). Only among diabetic women a significantly higher prevalence of increased IVS thickness, LVMI and left atrial diameter was found on intra-gender comparisons (Table 2, Figures 1, 2, 3). The age adjusted relative risk for increased LVMI in diabetics vs nondiabetics was 1.47 (95% CI: 1.0–2.2) in females and only 0.8 (0.5–1.3) in males.

Table 1: Baseline characteristics of the study population: number (%) or mean \pm standard deviation

Variables	MEN		WOMEN	
	Non DM n = 206	T2DM n = 108	Non DM n = 154	T2DM n = 92
Age (years)	65.8 \pm 6.2	65.9 \pm 5.6	60.0 \pm 6.9	61.0 \pm 6.2
Weight (kg)	80.7 \pm 13	82.3 \pm 13.2	76.0 \pm 12.4	76.7 \pm 13.2
HTN duration	10.7 \pm 8.8	10.7 \pm 8.7	12.3 \pm 9.4	14.8.0 \pm 9.4
Prevalent CAD	49 (25)	22 (21)	13 (8)	11 (12)
Current smokers	50 (25)	14 (13)	18 (11)	8 (9)
SBP (mm Hg)	170 \pm 21	174 \pm 19	170 \pm 18	173.6 \pm 23
DBP (mm Hg)	95.2 \pm 12	95 \pm 9.8	94.8 \pm 9.6	92.1 \pm 11.3
LVMI (g/m ²)	119.4 \pm 30	116.5 \pm 26	105.6 \pm 24	112.5 \pm 29*

SBP, DBP – systolic and diastolic blood pressures on inclusion; CAD – coronary artery disease; HTN duration-duration of hypertension (years); T2DM – type 2 diabetes mellitus; * $p < 0.05$.

Table 2: Echocardiographic data in study patients

Variables	MEN		WOMEN	
	Non DM n = 206	T2DM n = 108	Non DM n = 154	T2DM n = 92
IVS \geq 12 mm	123 (60)	66 (61)	63 (41)	51 (56)*
PW \geq 12 mm	36 (17)	17 (16)	13 (8)	12 (13)
Increased LVMI	55 (27)	21 (19)	53 (35)	45 (49)*
LA \geq 40 mm	100 (49)	60 (56)	42 (27)	40 (44)**

* $p < 0.05$, ** $p < 0.001$; IVS = interventricular septum, PW = posterior wall, LVMI = LV mass index > 110 (female) and > 134 gr/m²(male); LA = left atrial diameter; T2DM – type 2 diabetes mellitus. Data are number (%) of patients.

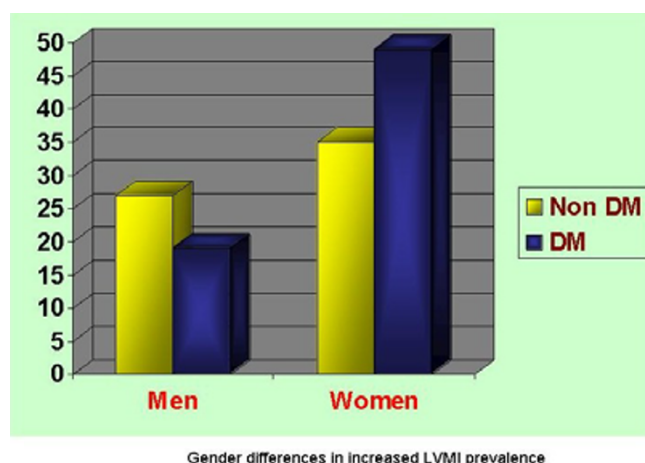
Discussion

In the present study diabetes mellitus was associated with increased prevalence of LVH (in terms of increased LVMI and IVS) in hypertensive women. LVH is more than just an adaptive response to hypertension. It is predictor a poor prognosis, independently of blood pressure levels. In the Framingham, the relative risk of cardiovascular mortality for every 50 g increment in echo LV mass was 1.73 in men and 2.12 in women, even after correction for risk factors such as blood pressure [2]. In patients with established CAD, the extra risk for cardiac death due to LVH is 2.8, when adjusted for age, gender and hypertension [3]. In these patients, this extra risk due to echo LVH appears to be greater than that for multivessel coronary disease or to LV dysfunction.

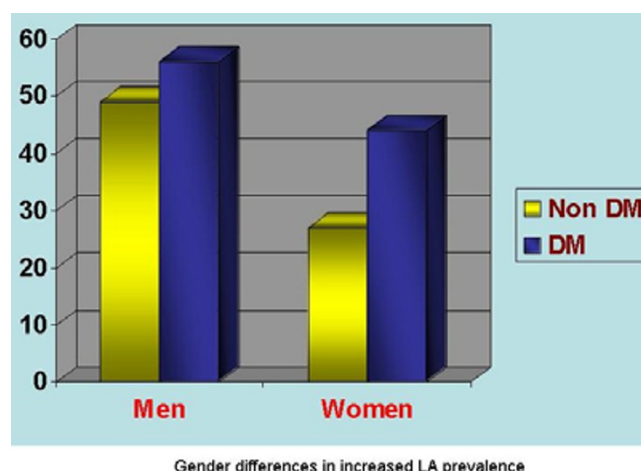
Recently, the close relationship between glucose metabolism abnormalities and other cardiovascular risk factors and diseases was emphasized [18-20]. In a previous study, LVH was present in 31% of diabetics, and systolic blood pressure was of no value in identifying those diabetics who had LVH [21], possibly because insulin resistance

itself stimulates LVM growth [22]. Verdecchia et al. supposed that in addition to circulating insulin, insulin growth factor-1 is also an independent determinant of LVM and geometry in essential hypertension [9]. However, Galvin et al. concluded that insulin resistance and hyperinsulinemia are not independent predictors of left ventricular mass in humans [11]. In a relatively healthy, population-based sample of hypertensive adults, type 2 diabetes was associated with higher LVM, more concentric LV geometry, and lower myocardial function, independently of age, sex, body size, and arterial blood pressure [10]. In the present study, similarly to Framingham cohort [23], diabetes was associated with higher LV mass in women but not in men. In addition, the prevalence of patients with increased left atrium diameter was significantly higher among diabetic women. We assumed that the latter phenomenon may be associated with increasing left atrial filling pressure following more pronounced LVH-related diastolic dysfunction.

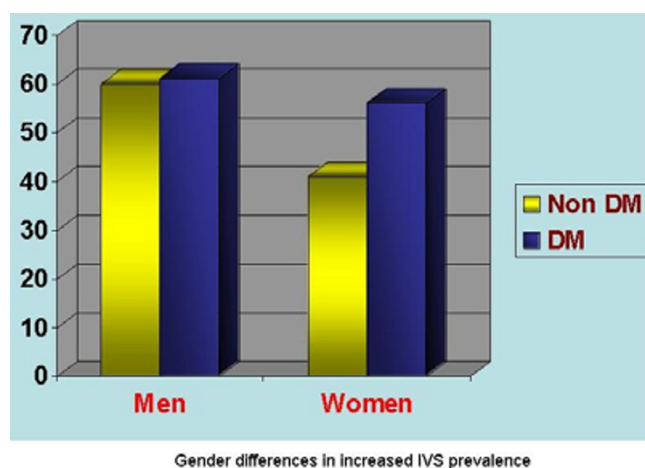
It is well established that diabetic women present a greater risk for cardiovascular morbidity and mortality compared

**Figure 1**

Gender differences in increased left ventricular mass index (LVMI) prevalence (percent). Diabetic women present a larger LVMI than nondiabetic women, while opposite results are seen in men.

**Figure 3**

Gender differences in increased left atrial (LA) prevalence (percent). Both diabetic women and diabetic men present a larger LA than their nondiabetic counterparts, but differences are significant only for women.

**Figure 2**

Gender differences in increased interventricular septal thickness (IVS) prevalence (percent). Both diabetic women and diabetic men present a larger IVS than their nondiabetic counterparts, but differences are significant only for women.

to their male counterparts [24-26]. In this context, our findings could represent an important component of the underlying mechanism.

Whether diabetes is associated with changes in left heart structure independently of blood pressure and metabolic

abnormalities remains to be elucidated in large prospective population-based studies.

Conclusion

Type 2 diabetes mellitus was associated with a significantly higher prevalence of LVH and left atrial enlargement in hypertensive women.

List of abbreviations

CAD: coronary artery disease; INSIGHT: Intervention as a Goal in Hypertension Treatment; IVS: interventricular septal thickness; LV: left ventricle; LVMI: left ventricular mass index; LVH: left ventricular hypertrophy.

Competing interests

None declared.

Authors' contributions

AT and JS envisioned the concept and prepared the initial draft of the article. AT, EZF and MM carried out the echocardiographic studies. EZF, ES, YA and MM critically revised the manuscript for important intellectual content. MB performed the statistical analysis. All authors read and approved the final version of the manuscript.

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